REMARKS

Reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 1-12 are pending in the application. Claims 1-12 stand rejected.

Rejections under 35 U.S.C. § 103

Claims 1-12 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Wesley et al., *The Plant Journal*, 2001 , Vol 27 no. 6, pp. 581-590 in view of Yukawa et al., *Plant Molecular Biology*, 2002, Vol 50, pp 713-723, and Applicants Specification. The Examiner has asserted that the rejection has been maintained for the reasons of record set forth in the Official Actions mailed 1/25/2007 and 10/22/2007.

Applicants maintain their position that the prior art fails to establish a prima facie case of obviousness for the reasons that have previously presented. Applicants remarks below are directed to particular points where there appears to be persistent misapprehension by the Examiner.

In particular, Applicants re-emphasize that Yukawa et al only demonstrated that plant 7SL RNA genes with inserted antisense RNA or ribozyme sequences are transcribed in an in vitro transcription system in a homologous plant extract. See Yukawa et al. at abstract line 7, page 714, bridging columns 1-2, or page 719, 2nd column lines 19-20. Yukawa et al. does not provide any evidence regarding how well chimeric genes comprising a type 3 Pol III promoter will actually be expressed in vivo in plant tissues.

On the basis of these limited experiments, Yukawa et al. indicate that 7SL RNA genes may be employed as potential cassettes for the expression of antisense RNA and ribozyme

sequences (page 713, Abstract, last sentence) or that "the new class of active chimeric pol III genes established here should be an important alternative to the well-studied tRNA genes as vehicles for antisense RNA expression in future experiments." (page 722, Discussion, last sentence).

Applicants particularly wish to direct the Examiner's attention to the word "genes" in both citations. It must be appreciated that Yukawa et al. did not demonstrate that isolated 7SL RNA promoters may be used to express antisense RNA or ribozymes. Rather, Yukawa et al. employed entire 7SL RNA genes wherein foreign sequences have been inserted "near the end of the 3'end of the coding region" (page 722, lines 5-7). See also Figure 5, page 720. The chimeric constructs when transcribed give rise to complete 7SL RNA wherein additional sequences have been inserted near the 3' end. Since the rationale behind the experiments described by Yukawa et al. was indeed to control in future experiments the localization of the inserted sequences (antisense or ribozymes – see abstract, page 713, last sentence; page 722, 1st column, last paragraph of the Discussion) such design made sense to reduce influence on SRP protein binding (page 722 lines 2 to 5). However, it is important not to overlook the fact that this is not tantamount to demonstrating that the 7SL RNA promoter elements are localized upstream of the transcription start point, since the chimeric constructs described by Yukawa et al. also contained all the sequences included in 7SL RNA downstream of the transcription start point.

This observation is particularly important as it demonstrates clear error in the dismissal by the Examiner of Applicants' arguments concerning the fact that the instantly claimed invention is unanticipated in view of the specification, claims, and the supporting remarks in the declaration of Dr Wang that his results are entirely unexpected. The Examiner has asserted that Applicants arguments were not persuasive because "Yukawa teaches a

significant advantage of the type 3 Pol III promoter over the type 2 Pol III promoter is that the type 3 POL III promoter does not have internal promoter, that are sequences that fall within the coding region of their respective genes, as is the case with type II promoters." This asserted basis for maintaining the rejection is clearly mistaken.

It appears that the Examiner has either misapprehended Applicant's arguments or has confused type II (sic - type 2 POL III) promoters with POL II promoters. Yukawa did not demonstrate that the 7SL RNA promoters can be used to transcribe antisense or ribozyme sequences. At best, Yukawa suggests that the 7SL promoter is a type 3 promoter which very likely encodes promoter elements that are localized upstream of the transcription start point (page 721, 2nd column, last paragraph), which is in contrast to the type 1 or type 2 POL III promoters.

Indeed, Applicants' argument was that chimeric constructs encoding short hairpin double-stranded RNA comprising a promoter recognized by RNA Polymerase III and comprising all cis-acting promoter elements which interact with DNA dependent RNA polymerase III (i.e. a type 3 POL III promoter) are unexpectedly more efficient in reducing gene expression of the target gene than a chimeric constructs under control of a promoter recognized by RNA polymerase II, such as a CaMV35S promoter. (Applicants have not presented any comparative data concerning chimeric constructs comprising a type 2 POL III promoter, nor have they made any representations concerning such chimeric genes and the relative efficiency compared to type 3 POL III containing chimeric constructs.)

The Examiner surely must realize that POL II promoters, like type 3 POL III promoters only contain promoter elements that are localized upstream of the transcription start point. Accordingly, Examiners remark that "Yukawa teaches a significant advantage of the type 3 Pol III promoter over the type 2 Pol III promoter is that the type 3 POL III

promoter does not have internal promoter, that are sequences that fall within the coding region of their respective genes, as is the case with type II promoters" is not a reason to dismiss applicants arguments.

In other words, since type 3 POL III promoters and POL II promoters have similar characteristics with regard to promoter localization, which seems to have been considered important by the Examiner, the Examiner's observation actually reinforces Applicants' point that there would have been no a priori reason to expect type 3 POL III promoters to be more efficient than POL II promoters. That is why the results obtained with the chimeric constructs as currently claimed are surprising. The failure of the prior art to appreciate the surprising results provided by the claimed invention relative to the use of the commonly used constitutive plant promoter CaMV35S. The unexpected efficiency that is provided by the presently claimed combination relative to the conventional promoter is objective evidence of non-obviousness that does not appear to have been given adequate consideration.

Applicants maintain that the cited references would not have allowed a skilled person to predict that type 3 Pol III promoters are more effective than a CaMV35S promoter for gene silencing with relatively short hairpin sequences. At the time of the invention, a large variety of promoters of various types would have been known to a person of ordinary skill in the art. However, the state of the art regarded the CaMV35S promoter as a strong constitutive promoter for directing expression in plants. Absent any specific evidence that another type of promoter would provide significantly better results than the CaMV35S, there would have been no motivation for a person of ordinary skill to use a different promoter. In particular, there would have been no reason for a person of ordinary skill in the art to select the type 3 polymerase III promoters that are recited in the claims of the present application over any of the several other types of promoter for use instead of the CaMV35S promoter.

It is improper for the Office to disregard the results achieved by the claimed combination. An analysis of obviousness of a claimed combination must include consideration of the results achieved by that combination. *The Gillette Co. v. S.C. Johnson & Son Inc.,* 16 USPQ2d 1923, 1928 (Fed. Cir. 1990). Critical to the analysis is an understanding of the particular results achieved by the new combination. *Id.* (citing *Interconnect Planning Corporation v. Feil,* 227 U.S.P.Q. 543, 551 (Fed. Cir 1985)). Applicants submit that an analysis that takes appropriate account of the substantial improvement that the inventors have accomplished with the claimed invention must conclude that the invention was not obvious. Absent any disclosure predicting the significant improvements afforded by the present invention, there would have been no reason to modify the teachings of Wesley et al. to make the present invention. Thus, the surprising benefits afforded by the present invention do comprise a secondary consideration that demonstrates that the invention would not have been obvious.

For at least the foregoing reasons, reconsideration and withdrawal of the remaining rejection in this application is respectfully requested.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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